

In the description:

The paragraph beginning on page 3, line 27 is amended as follows:

The therapeutic compounds described below comprise very small capsules which can be injected into body tissue, particularly the heart. The capsules include an encapsulating layer which surrounds a therapeutic agent. After injection, the encapsulating layer degrades or dissolves, and the therapeutic agent is released within the heart. The therapeutic agent may be one of any number of known agents such as anti-arrhythmic drugs, gene therapy solutions, and macromolecules intended to have either acute or long-term effects on the heart. While some of these therapeutic agents are used to treat the heart by injecting them into the heart, they are of such small size that they readily enter the cardiac capillary system and the cardiac lymphatic system, and are quickly transported away from the injection site. Thus, in prior treatment methods, relatively large doses and repeated ~~doses~~ doses are required to provide therapeutic effect at the injection site. To provide a solution to this problem, the capsules described below are provided in sizes that are too large to permit capillary transport or lymphatic transport. Thus, injected capsules are immobile within the heart tissue, and upon degradation they will release a therapeutic agent very near the site of injection. The capsules may also be provided in sizes that are too large to permit capillary transport, but small enough to enter the lymphatic system and be transported away from the injection site in the cardiac lymphatic system, so that the therapeutic effect is provided at some distance from the injection site. The encapsulating layer may be made from various materials including biodegradable polymers in the form of microspheres, or from standard vesicle forming lipids which form liposomes and micelles.

Please add the following two paragraphs just before the Detailed Description of the Invention on page 5, line 6 and after page 5, line 5:

Figure 6 is a like view showing the balloon angioplasty.

Figure 7 is a like view showing a deployed stent.

The paragraph beginning on page 19, line 4 is amended as follows:

The ability to deposit therapeutic agents in to the myocardium for uptake into the cardiac lymphatic system, combined with the ability of some of the molecules discussed above to migrate from the lymphatic ducts into parallel running arteries, permits introduction of therapeutic agents for the coronary arteries to be introduced through this pathway. The result is a very low flow environment for the introduction of anti-stenotic compounds and other arterial therapeutic agents, as compared to the infusion of therapeutic agents into the high flow environment of the coronary arteries themselves. The method illustrated in Figure 5 is useful to deliver therapeutic agents to the coronary arteries, such as the left coronary artery and its branches, including the left anterior descending coronary artery, and the right coronary artery and its branches. As illustrated in Figure 5, catheter system 9 with centrally located drug delivery catheter 20 implanted at a depth within the left ventricular apex 15 of the heart 10. Hollow penetrating structure 30 has penetrated the heart muscle from the endocardial side. The artery to be treated, in this case the circumflex branch of the left coronary artery 500, courses over the surface of the heart (chosen for illustration purposes only). A corresponding epicardial lymphatic vessel 501 runs nearby, and many sub-epicardial lymphatic vessel such as vessel 502 drain into the epicardial lymphatic vessel. (It should be noted that the cardiac lymphatic vessels are both numerous and largely uncharted, and may be highly variable from

person to person). The artery is occluded by an arterial plaque, cholesterol or stenotic mass 505 which is amendable to treatment with drug therapies. The artery may have been previously treated with angioplasty, or a stent may have been placed across the occlusion. For example, balloon angioplasty is illustrated in Figure 6, which shows an angioplasty catheter 520 with a balloon 521 mounted its distal tip, placed within the artery 500 in the area of a lesion (mass 505, for example). Expansion the lesion with the angioplasty balloon may precede treatment with catheter 510. Likewise, as illustrated in Figure 7, a stent 530 may be placed within the region of the blood vessel occluded by a lesion (mass 505, for example). Both methods of treatment are often accompanied by injury to the surrounding blood vessel and restenosis. In any case, several drugs are available to either ameliorate the blockage or prevent restenosis or re-occlusion after balloon angioplasty and/or stent placement. The delivery catheter is navigated into the endocardial space of the left ventricle 510, and secured in place with penetrating structure 30. A small dose of therapeutic agent, indicated by the molecules 35, is injected into the myocardium, and the penetrating structure is withdrawn. (Withdrawal of the penetrating structure may be delayed as necessary to prevent the therapeutic agent from draining back into the ventricular space.) The molecules of the therapeutic agent are taken up by the lymphatic system, entering into vessels 501 and 502, and transported upwardly. The molecules also migrate out of the lymphatic system and then migrate into the nearby coronary artery, following multiple paths indicated by the arrows in Figure 5. The molecules penetrate the adventicia, or outer layer, of the coronary artery, and thus enter the coronary artery. Molecules enter the coronary artery along the entire length that runs near the lymphatic vessels which initially take up the molecules. Thus, therapeutic agent enters the coronary blood vessel at the site of occlusion and proximally to the occlusion, after having been injected into a more distal location (relative to the coronary artery). The term entering the artery

may include entering the arterial wall without entering the lumen of the artery, or passing through the arterial wall into the lumen of the artery. While the method is illustrated in relation to the left circumflex coronary artery, it may be used with all the coronary arteries. Also, while endocardial access is preferred for the method as applied to the coronary arteries located on the anterior surface of the heart (left and right coronary arteries). Therapeutic agents may be deposited into the myocardium through catheters delivered into the coronary sinus, the coronary veins, and even the coronary arteries, including the coronary artery subject to treatment by angioplasty or stent placement. Additionally, while it is preferable to accomplish the therapy percutaneously, the method may be accomplished by injection into the heart, epicardially, during open surgery, or during endoscopic or key-hole surgery through the chest.

In the drawings:

Please add Figures 6 and 7 as attached to this preliminary amendment. Figures 6 and 7 were a part of the parent application and add no new matter to this application.